decreased breakthrough allergic symptoms. Based on our findings, this option may be particularly appropriate for individuals with allergy who predominantly produce IgE to 2S albumins. A controlled trial of tolerance induction using boiled peanut in patients allergic to peanut is required to investigate this further, before this can be recommended as a potential treatment modality.

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REFERENCES

1. Nowak-Wegrzyn A, Bloom KA, Sicherer SH, Shreffler WG, Noone S, Wanich N, et al. Tolerance to extensively heated milk in children with cow's milk allergy. J Allergy Clin Immunol 2008;122:342-7.
2. Martos G, Lopez-Exposito I, Bencharitiwong R, Berin MC, Nowak-Węgrzyn A. Mechanisms underlying differential food allergy response to heated egg. J Allergy Clin Immunol 2011;127:990-7.
3. Turner PJ, Wong M, Varese N, Rolland JM, O'Hehir RE, Campbell DE. Tolerance to wheat in whole-grain cereal biscuit in wheat-allergic children. J Allergy Clin Immunol 2013;131:920-3.
4. Shek LP, Cabrera-Morales EA, Soh SE, Gerez I, Ng PZ, Yi FC, et al. A population-based questionnaire survey on the prevalence of peanut, tree nut, and shellfish allergy in 2 Asian populations. J Allergy Clin Immunol 2010; 126:324-31, 331.e1-7.
5. Beyer K, Morrow E, Li XM, Bardina L, Bannon GA, Burks AW, et al. Effects of cooking methods on peanut allergenicity. J Allergy Clin Immunol 2001;107: 1077-81.
6. Blanc F, Vissers YM, Adel-Patient K, Rigby NM, Mackie AR, Gunning AP, et al. Boiling peanut Ara h 1 results in the formation of aggregates with reduced allergenicity. Mol Nutr Food Res 2011;55:1887-94.
7. Vissers YM, Blanc F, Skov PS, Johnson PE, Rigby NM, Przybylski-Nicaise L, et al. Effect of heating and glycation on the allergenicity of 2S albumins (Ara h 2/6) from peanut. PLoS One 2011;6(8):e23998.
8. Marsh J, Rigby N, Wellner K, Reese G, Knulst A, Akkerdaas J, et al. Purification and characterisation of a panel of peanut allergens suitable for use in allergy diagnosis. Mol Nutr Food Res 2008;52(suppl 2):S272-85.
9. Mondoulet L, Paty E, Drumare MF, Ah-Leung S, Scheinmann P, Willemot RM, et al. Influence of thermal processing on the allergenicity of peanut proteins. J Agric Food Chem 2005;53:4547-53.

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Peanut allergy prevalence among school-age children in a US cohort not selected for any disease

To the Editor:

What is the prevalence of peanut allergy among US children? Given that 90% of US households consume peanut butter,[1] this is an important question. The answer is not straightforward, however, as estimates of peanut allergy prevalence among US children differ by allergy definition, study population, and methodology.[2] Previous estimates for US children have been based on self-report[3-6] or specific IgE (sIgE) criteria,[7] which are thought to be inaccurate.[2] Estimates have varied according to whether they were based on telephone surveys,[3] electronic surveys,[4] or nationally representative surveys such as the National Health and Nutrition Examination Survey (NHANES) (Table I).[5-7] One must consider that self-report is hindered by reporting bias, surveys of food allergy are more likely to enlist those with the condition, and nationally representative surveys are limited in the extent of phenotyping possible given their wide scope. It can therefore be difficult to discern how differences in definition, study population, and methodology affect prevalence estimates across studies. Here we report and compare prevalence estimates of childhood peanut allergy according to varying criteria among 7- to 10-year-old children participating in a US birth cohort not selected for any disease.

We determined prevalence of childhood peanut allergy based on reported symptoms, sIgE levels, clinical information, and combinations of these variables among participants of Project Viva. Project Viva is a large, observational cohort study based in eastern Massachusetts with enrollment from Harvard Vanguard Medical Associates, a multi-site group medical practice. Participants were not selected for any disease. The study was designed to examine maternal dietary and other factors that could influence child health outcomes, with health broadly defined.[8] Enrollment occurred between 1999 and 2002 in early pregnancy and resulted in delivery of 2128 singleton children. Interviews and questionnaires on child health were administered when the children were age 6 months, 1 year, and annually thereafter. We collected outcome data for this study at the mid-childhood in-person visit (mean age 7.9 years). Among the 1277 children who presented for an in-person interview at mid-childhood, 699 (55%) had blood drawn, and 616 (87.7% of those with blood samples) had sIgE measured by ImmunoCAP (Phadia AB, Uppsala, Sweden). Compared with those who did not follow up, participants who did follow up showed higher proportions of maternal white race (69% vs 62%), college or graduate education (69% vs 58%), and annual household income ≥ $70,000 (63% vs 58%), but there were no significant differences in parental atopy ($P = .13$). Compared with the general US population, there was a higher proportion of blacks and lower proportion of Hispanics among participants. Further details regarding the comparability

TABLE I. Previously reported prevalence estimates of childhood peanut allergy in the US

Study	Criteria for definition	Method	Survey year	Prevalence percent (95% CI)
Sicherer et al[2]	Self-reported reaction and symptoms	Telephone survey	1997	0.4 (0.2-0.7) in <18 y
Sicherer et al[2]	Self-reported reaction and symptoms	Telephone survey	2002	0.8 (0.5-1.2) in <18 y 0.8 (0.4-1.8) in 6-10 y
NHANES 2005-2006[7]	Clinical food allergy based on sIgE criteria*	Nationally representative survey	2005-2006	1.8 (1.5-2.1) in 1-5 y 2.7 (2.4-3.0) in 6-19 y
NHANES 2005-2006[7]	Peanut sIgE ≥ 14 kU/L†	Nationally representative survey	2005-2006	1.0 (0.7-1.3) in 1-5 y 0.9 (0.7-1.2) in 6-19 y
NHANES 2007-2008[6]	Self-reported allergy‡	Nationally representative survey	2007-2008	1.4 (0.9-1.9) in <18 y
Sicherer et al[2]	Self-reported reaction and symptoms	Telephone survey	2008	1.4 (1.0-1.9) in <18 y 2.1 (1.3-3.4) in 6-10 y
NHANES 2009-2010[6]	Self-reported allergy‡	Nationally representative survey	2009-2010	0.9 (0.4-1.4) in <18 y
NHANES 2007-2010[6]	Self-reported allergy‡ excluding those with recent consumption	Nationally representative survey	2007-2010	0.9 (0.7-1.1) in children and adults
Infant Feeding Practices Study II[5]	Self-reported allergy	Mail survey	2009-2010	0.6 (0.3-1.0) in <1 y
Gupta et al[4]	Self-reported allergy and reaction history	Electronic survey	2009-2010	2.0 (1.8-2.2) in < 18 y 1.9 (1.6-2.3) in 6-10 y

*As defined by Liu et al as 50% of participants with peanut sIgE 2.0-14.0 kU/L and 95% of participants with peanut sIgE ≥ 14 ku/L.[7]
†90% specificity decision point reported by Sampson.[10]
‡Based on broad questions that did not address symptoms.[5,6]

TABLE II. Prevalence of peanut allergy among school-age children in a US observational birth cohort not selected for any disease (N = 616)

Criteria for definition	No.	Prevalence percent (95% CI)
Self-reported reaction and symptoms	27	4.6 (2.9-6.3)‡
Clinical food allergy based on sIgE criteria*	31	5.0 (3.5-7.1)
Peanut sIgE ≥ 0.35 kU/L and prescribed epinephrine auto-injector	29	4.9 (3.2-6.7)‡
Peanut sIgE ≥ 14 kU/L†	18	2.9 (1.6-4.3)
Peanut sIgE ≥ 14 kU/L and prescribed epinephrine auto-injector	12	2.0 (0.9-3.2)‡

*As defined for NHANES by Liu et al as 50% of participants with peanut sIgE 2.0-14.0 kU/L and 95% of participants with peanut sIgE ≥ 14 ku/L.[7]
†90% specificity decision point reported by Sampson.[10]
‡Denominator is 589 subjects with complete interview responses.

of the 616 children to the larger cohort have been previously described.[8]

We considered a child to have self-reported peanut allergy if his or her mother answered yes to the question, "Has your child ever had an allergic reaction to peanuts?" *and* yes to questions about at least 1 of the following categories of allergic reaction symptoms with peanut ingestion: "skin-related (eg, hives, swelling)," "respiratory (eg, shortness of breath, wheezing, cough)," "cardiovascular (eg, low blood pressure, dizziness or fainting)," "gastrointestinal (eg, vomiting, diarrhea)," or "anaphylaxis (severe, multi-system allergic reaction)." These questions, which assess convincing symptoms of IgE-mediated reaction, are comparable to those used in previous studies of self-reported peanut allergy by Sicherer, et al.[3] We assessed prescription of an epinephrine auto-injector with the question, "Has a health care professional, such as a doctor, physician assistant or nurse practitioner, ever prescribed an EpiPen for your child?"

The prevalence of self-reported peanut allergy in this cohort of US children not selected for any disease was 4.6% (Table II), higher than previously reported estimates of self-reported peanut allergy among US children of comparable age (Table I). Similarly, we observed a 5.0% prevalence of "clinical peanut allergy" according to sIgE-based criteria that previously resulted in a 2.7% prevalence among comparably aged children in the 2005 to 2006 NHANES study.[7] Within Project Viva, the 4.9% prevalence of peanut allergy defined by both sensitization and prescribed epinephrine auto-injector was similar in magnitude to the estimates defined by self-reported allergy and sIgE-based "clinical allergy" criteria.

The relatively high prevalence rates we observed may reflect continued rise of peanut allergy prevalence in the US, consistent with the rising trend in self-reported peanut allergy that Sicherer, et al observed between 1997, 2002, and 2008.[3] Additionally, our cohort was based in the Northeast, where rates of peanut sensitization may be higher relative to western US regions.[9]

Application of a more stringent definition of peanut allergy than self-reported allergy or "clinical allergy," such as the peanut sIgE ≥ 14 kU/L decision point for 90% specificity reported by Sampson,[10] yielded a prevalence of 2.9% (Table II), which is still higher than previously reported estimates by any criteria (Table I). Our strictest definition of peanut allergy, requiring peanut sIgE greater than the 90% specificity decision point *and* prescribed epinephrine auto-injector, yielded a prevalence of 2.0%. While it could be argued that despite Project Viva's general health goals, the relatively high prevalence rates we observed could be due to families with food allergies preferentially returning for mid-childhood visits, the rates of parental atopy (assessed prenatally) among those who did and did not present at mid-childhood were not significantly different, supporting that selection bias was not at play.

As we assessed peanut allergy using different criteria within this cohort, we also assessed for agreement between the definitions. Agreement was the highest between self-reported peanut allergy and peanut allergy defined by both peanut sensitization and prescribed epinephrine auto-injector ($\kappa = 0.75$, 95% CI 0.62-0.88). There was moderate agreement between self-reported peanut allergy and peanut allergy defined by both the 90% specificity decision point and prescribed epinephrine

auto-injector (κ = 0.57, 95% CI 0.38-0.76), and less agreement between self-reported peanut allergy and peanut allergy defined by the 90% specificity decision point only (κ = 0.49, 95% CI 0.31-0.68).

Each epidemiologic method for assessing peanut allergy prevalence has strengths and limitations. Double-blind, placebo-controlled food challenges are the gold standard for clinical peanut allergy diagnosis, but these are challenging to implement in large, unselected cohorts and have not been done in unselected US cohorts.[2] As diagnostic adjuncts, component resolved diagnostics may also be increasingly implemented in epidemiologic cohorts going forward. In this letter, we have provided prevalence estimates according to several criteria that can be compared to one another and to previous estimates. Our results come from a US cohort of children not selected for allergy or any disease, and they support that peanut allergy is an increasingly prevalent condition.

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REFERENCES

1. National Peanut Board. National Peanut Board Fun Facts. http://nationalpeanutboard.org/the-facts/fun-facts/. Accessed March 12, 2014.
2. Sicherer SH, Sampson HA. Food allergy: Epidemiology, pathogenesis, diagnosis, and treatment. J Allergy Clin Immunol 2014;133:291-307.
3. Sicherer SH, Munoz-Furlong A, Godbold JH, Sampson HA. US prevalence of self-reported peanut, tree nut, and sesame allergy: 11-year follow-up. J Allergy Clin Immunol 2010;125:1322-6.
4. Gupta RS, Springston EE, Warrier MR, Smith B, Kumar R, Pongracic J, et al. The prevalence, severity, and distribution of childhood food allergy in the United States. Pediatrics 2011;128:e9-17.
5. Keet CA, Savage JH, Seopaul S, Peng RD, Wood RA, Matsui EC. Temporal trends and racial/ethnic disparity in self-reported pediatric food allergy in the United States. Ann Allergy Asthma Immunol 2014;112:222-9.e3.
6. McGowan EC, Keet CA. Prevalence of self-reported food allergy in the National Health and Nutrition Examination Survey (NHANES) 2007-2010. J Allergy Clin Immunol 2013;132:1216-9.e5.
7. Liu AH, Jaramillo R, Sicherer SH, Wood RA, Bock SA, Burks AW, et al. National prevalence and risk factors for food allergy and relationship to asthma: results from the National Health and Nutrition Examination Survey 2005-2006. J Allergy Clin Immunol 2010;126:798-806.e13.
8. Bunyavanich S, Rifas-Shiman SL, Platts-Mills TA, Workman L, Sordillo JE, Camargo CA Jr, et al. Peanut, milk, and wheat intake during pregnancy is associated with reduced allergy and asthma in children. J Allergy Clin Immunol 2014;133:1373-82.
9. Salo PM, Arbes SJ, Jr, JaramilloR, Calatroni A, Weir CH, Sever ML, et al. Prevalence of allergic sensitization in the United States: Results from the National Health and Nutrition Examination Survey (NHANES) 2005-2006 [published online ahead of print February 9, 2014]. J Allergy Clin Immunol doi: 10.1016 /j.jaci.2013.12.1071.
10. Sampson HA. Utility of food-specific IgE concentrations in predicting symptomatic food allergy. J Allergy Clin Immunol 2001;107:891-6.

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Galactose-alpha-1,3-galactose sensitization is a prerequisite for pork-kidney allergy and cofactor-related mammalian meat anaphylaxis

To the Editor:

Delayed type I reactions to red meat are typical for patients sensitized to galactose-alpha-1,3-galactose (α-Gal), and increasing numbers of patients are being recognized worldwide.[1,2] Interestingly, allergic reactions to pork kidney are mainly observed in Europe and are a good example of how regional differences in meat consumption can influence the clinical presentation of this specific variant of type I allergy.[3] The aim of this study was to outline how an understanding of allergy to pork kidney can be helpful for the understanding of red meat allergy in general.

Based on clinical history, 25 German patients (9 female, 16 male; median age 56 years; Table I) with a history of at least 1 allergic reaction to pork kidney were selected and analyzed. The consumption of pork kidney led to anaphylaxis in 72% of the patients (according to the Ring and Messmer severity scale,[4] 56% of those were grade II, and 44% were grade III) and to urticaria/angioedema without extracutaneous manifestations in the remaining 28%. Using structured interviews, cofactors of anaphylaxis[5] could be identified in 81% of the patients (21/25 patients, Table I). Additional systemic allergic reactions to other mammalian meat, dairy products, or gelatin were reported in 56% of the patients (Table I). Based on the reported time between consumption of pork kidney and onset of the first symptoms, the reactions were classified as immediate type I reactions (≤3 hours) and delayed type I reactions (3 to 6 hours). In this cohort (n = 21; mean reaction time 1.25 hours; range 0.25 to 8.0 hours), 67% were immediate type I reactions. Interestingly, patients with a history of hypersensitivity to pork kidney only (n = 9; mean reaction time 3.5 hours; range 0.5 to 8.0 hours) were evenly distributed between the immediate type I reaction and the delayed type I reaction groups (ratio 1.25:1). In contrast, patients with hypersensitivity to both pork kidney and red meat (n = 11) reacted earlier, with an immediate type I reactions/delayed type I reactions ratio of 3:1 (mean reaction time 1.5 hours; range 0.25 to 5.0 hours). Two or more associated cofactors (ratio 3.5:1) and anaphylaxis (grades II and III) were linked to immediate type I reactions (ratio 2:1).

Commercially available skin prick tests from pork, beef, lamb, or horse meat extracts elicited reactions in only 2 patients, milk extracts in 0 patients. In contrast, prick-to-prick tests using raw and cooked pork kidney showed 100% sensitivity, higher than raw and cooked beef kidney and muscle meat of different species (Fig 1). The process of cooking beef and pork meat decreased sensitivity in prick-to-prick tests. The pattern of prick-to-prick test results was comparable in patients with only pork-kidney